Factors associated with HIV viral suppression among children and adults receiving antiretroviral therapy in Malawi in 2021: Evidence from the Laboratory Management Information System

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ABSTRACT

Objective: To describe the prevalence of HIV viral suppression and assess the factors associated with HIV viral suppression among persons receiving ART in Malawi in 2021.

Methods: Implementation study using routinely collected patient-level HIV RNA-PCR test result data extracted from the national Laboratory Management Information System (LIMS) database managed by the Department of HIV/AIDS in 2021. We calculated frequencies, proportions and odds ratios (OR) of HIV viral suppression with their associated 95% confidence intervals (95%CI). We performed a random-effects logistic regression to determine the risk factors associated with HIV viral suppression amongst ART patients, controlling for the spatial autocorrelation between districts and adjusting for other variables.

Results: We evaluated 515,797 adults and children receiving ART and having a viral load test in 2021. Of these, 92.8% had HIV viral suppression. ART patients living in urban areas had lower likelihood of HIV viral suppression than those living in rural areas (adjusted OR [aOR]=0.95, 95%CI: 0.92-0.99, P=0.01). There was an increasing trend in HIV viral suppression with increasing ART duration. Routine VL monitoring samples were 39% more likely to have suppressed VL values than confirmatory HIV VL monitoring samples (aOR=1.39; 95%CI:1.34-1.43, P<0.001).

Conclusion: This is the first national analysis of Malawi HIV VL data from LIMS. Our findings show the need to particularly consider the urban residents, those below 20 years, males, those on ART for less than a year as well as those on specific ARV regimens in order to persistently suppress HIV VL and consequently achieve the goal of achieving HIV VL suppression by 2030.

Keywords: HIV viral load, VL, Malawi, Treatment failure, HIV, ART, HIV viral suppression

INTRODUCTION

WHO has recommended immediate initiation of antiretroviral therapy (ART) for all people living with HIV since 2015 [1] [2]. The main benefit of ART is the suppression of HIV-1 viral replication [2] [4]. The suppression of viral load (VL) (defined by WHO as ⩽1000 HIV - RNA copies/mL) reduces morbidity and mortality among patients living with HIV and onward transmission of the virus [1]. Since 2013, WHO has recommended VL monitoring to detect treatment failure after ART

initiation [1] [2] [3]. WHO guidelines were further refined in 2016 and currently recommend routine VL testing yearly among patients stable on ART [2]. Patients on non-nucleoside reverse transcriptase inhibitor (NNRTI) based regimens with two consecutive unsuppressed VL measurements (>1000 copies/mL) despite enhanced adherence counselling, taken within a 3-month interval and at least 6 months after starting ART are considered to have treatment failure [1]. However, patients on integrase strand transfer inhibitor (INSTI) or protease inhibitor (PIs) based regimens need a genotype test after a high follow-up VL to distinguish treatment failure due to drug resistance from poor adherence [1].

Malawi achieved two of the three 90-90-90 targets of the 2020 Joint United Nations Programme on HIV/AIDS (UNAIDS). Overall 91% of the people living with HIV were aware of their status, 83% of those aware of their status were on ART, and 90% of those on ART were virally suppressed in 2020 [5]. Over the past decade, there has been an increasing trend in the number of persons starting ART in sub-Saharan Africa (SSA) [6]. Therefore, it is important to sustain treatment success and limit the development of treatment failure [6]. Despite WHO recommending routine uptake of VL monitoring since 2013, the uptake has been sub-optimal especially in SSA due to limited testing capacity or shortage of staff to conduct the testing [7]. Uptake of VL testing has varied across countries, depending also on age, antiretroviral drug regimen and sex. For example, the proportion of patients with at least one VL test by mid-2016 was 19% in Malawi, 11% in Cote d'Ivoire, 49% in Kenya, 43% in Namibia, 9% in Tanzania and 22% in Uganda. [2] [7].

The Malawi Ministry of Health (MoH) has been implementing routine VL monitoring since 2012. Before 2018, patients on ART were supposed to have an HIV VL every two years with the first one to be taken at six months after start of ART treatment (i.e., in months 6, 24, 48, 72, etc. for routine HIV VL assessment) [8]. Since 2018, ART patients are supposed to have a routine HIV VL test every year [9] [10]. The Malawi MoH therefore tracks the prevalence and incidence of VL suppression amongst the persons who are receiving ART [11]. Since the introduction of this program no in-depth analyses have been done to assess the prevalence of HIV viral suppression amongst the persons receiving ART at national level in Malawi. However, in-depth analyses are necessary for a greater understanding of HIV VL monitoring and its quality improvement as well as ensuring the achievement of the UNAIDS target of ending HIV/AIDS by 2030. This study therefore aims to describe the prevalence of HIV viral suppression, and assess the factors associated with trends in the prevalence of HIV viral suppression among persons that received ART in Malawi in 2021 using data from the Malawi Laboratory Management Information System (LIMS).

METHODS

Study design

We used patient-level HIV VL data from the LIMS national database containing data collected in 2021 in Malawi [12] since this was the most recent year with data for all 12 months. Furthermore, data on regimens were incorporated in the LIMS database from mid-2020. The LIMS database is a central data repository for all molecular laboratory tests in Malawi managed by the Diagnostics Department of the Ministry of Health. The LIMS database contains individual level HIV VL data from all districts and ART facilities in Malawi. The database has inbuilt tools for performing data quality assessment like range checks and other associated validation rules.

Data collection

The source of patient-level characteristics is the lab requisition forms that are filled by staff collecting the samples, usually the HIV Diagnostic Assistants (HDAs) [11]. This can be a considerable challenge as the HDAs are often not fully aware of the details of the regimen and other patient characteristics. Furthermore, the data are captured as a single entry by clerks at the lab receptions, which explains some of the gaps and obvious inconsistencies in the data.

The LIMS dataset has no reliable unique patient identifier, which makes it hard to identify sequential samples from the same patients. We were able to re-identify some patients on the basis of their characteristics from LIMS. This makes it obvious that many samples are mislabeled as "routine scheduled" when we can easily deduce that the interval from the last sample is too short for the scheduled monitoring milestones. Such samples are re-classified as "confirmatory" or "targeted". The routine HIV VL are currently being done yearly for a patient that has been on ART for at least 12 months. However, when a clinician has a suspicion that the patient may be failing on ART then a confirmatory VL is done.

Data Management

The data were managed in Stata v16.0 (Stata Corp., Texas, USA). All HIV VL data collected between 1 January 2021 and 31 December 2021 were included in this study. The response variable was suppressed VL (defined as having a VL below 1000 copies [13] [14]. The independent variables were: age at sample collection, sex, facility location (rural/urban), reason for VL testing (routine/targeted), current first-line ART regimen, sample type (plasma/dried blood spot (DBS)) and region (north/central/south).

Statistical Analysis

A descriptive analysis was first performed detailing the characteristics of the study population. We also fitted bivariate analysis of each of the independent variables and HIV viral suppression. We fitted a multivariable logistic regression model of HIV viral suppression, with HIV viral suppression clustered by district, using a forward step-wise selection method, with age and sex entered as a priori variables. Because the prevalence of HIV viral suppression varies by district, we controlled for random clustering effect of the district when conducting logistic regression of the independent variables on HIV viral suppression. We presented both crude and adjusted odds ratios (OR) of HIV viral suppression for each independent variable. Multiple imputation chained equations (MICE), with five imputation rounds and 5000 permutations, were used to impute missing data of the following covariables: age category (at the time the sample was taken), and sex of the patient. We calculated the within district variation (ρ) and between district variation (σ) of the prevalence of HIV viral suppression due to controlling for clustering effect of the district. We presented the prevalence of HIV viral suppression for all the districts of Malawi using a forest plot of the pooled prevalence of HIV viral suppression in order to get the degree of heterogeneity of the HIV viral suppression across districts. Statistical significance was set at $P<0.05$.

Ethics approval

The study was approved by the Malawi National Health Sciences Research Committee (NHSRC) in Lilongwe, Malawi (protocol#:1669). As this study used secondary anonymized data, no informed consent was needed.

RESULTS

Characteristics of the study participants

The characteristics of adults and children that accessed ART and had HIV VL assessment in Malawi in 2021 are shown in Table 1. We included 515,797 adults and children receiving ART and having a viral load test in 2021. Of these, 58% were females; 7% were aged below thirteen years while 88% were aged twenty and above, 64% were from rural areas; 10% from the northern region and 65% from the southern region. Overall, 1% accessed HIV care at health facilities managed by private companies while 77% accessed HIV care from public facilities (Table 1). Overall, 15% of the VL samples were plasma while 85% were DBS VL samples; and 9% of the VL samples were targeted (to confirm suspected treatment failure) and 91% were taken during routine scheduled monitoring visiting. The median age at VL sample draw was 41 years (inter-quartile range (IQR): 31-50). The majority of patients (n=322,483, 63%) were on TDF/3TC/DTG while for 34% of 515,797 patients the ARV regimens was missing.

Table 1: Characteristics of adults and children that received antiretroviral therapy and had HIV viral load testing in Malawi in 2021

Patient characteristics	n (%)
Total	515,797 (100.0)
Sex	
Male	181,127 (35.1)
Female	299,951 (58.2)
Missing	34,719 (6.7)
Location	
Rural	323,998 (62.8)
Urban	191,799 (37.2)
Age at sample draw (in years)	
0-12	37,120 (7.2)
13-19	23,617 (4.6)
20+	455,060 (88.2)
Region	
Northern	48,997 (9.5)
Central	132,255 (25.6)
Southern	334,545 (64.8)
Months on antiretroviral therapy	
6-11	28,946 (5.6)
12-23	30,600 (5.9)
24-35	32,752 (6.4)
36-47	32,738 (6.4)

48-59	35,250 (6.8)
60+	237,424 (46.0)
Missing	118,087 (22.9)
Managing authority of facility	
Faith-based	86,329 (16.7)
Company	4,546 (0.9)
Government	395,019 (76.6)
NGO	9,819 (1.9)
Private	20,084 (3.9)
Type of sample	
DBS	437,716 (84.9)
Plasma	78,081 (15.1)
Reason for viral load sample	
Confirmatory	44,491 (8.6)
Routine	470,542 (91.2)
Missing	764 (0.2)
ARV regimens	
0P (ABC/3TC+NVP)	30 (<0.1)
0A (ABC/3TC+NVP)	39 (<0.1)
2P (AZT/3TC/NVP)	978 (0.2)
4A (AZT/3TC+EFV)	225 (<0.1)
5A (TDF/3TC/EFV)	1,773 (0.3)
6A (TDF/3TC+NVP)	167 (<0.1)
7A (TDF/3TC+ATVr)	497 (0.1)
8A (AZT/3TC+ATVr)	952 (0.2)
9P (ABC/3TC+LPVr)	3,353 (0.7)
9A (ABC/3TC+LPV/r)	661 (0.1)
10A (TDF/3TC+LPVr)	201 (<0.1)
11P (AZT/3TC+LPVr)	264 (0.1)
11A (AZT/3TC+LPVr)	207 (<0.1)
12A (DRVr+DTG)	622 (0.1)
13A (TDF/3TC/DTG)	322,483 (62.5)
14P (AZT/3TC+DTG)	191 (<0.1)
14A (AZT/3TC+DTG)	2,534 (0.5)
15P (ABC/3TC+DTG)	2,145 (0.4)
15A (ABC/3TC+DTG)	2,520 (0.5)
16P (ABC/3TC+RAL)	80 (<0.1)

Missing	175,875 (34.1)

ABC= Abacavir; 3TC= Lamivudine; NVP= Nevirapine; AZT= zidovudine; EFV= efavirenz; TDF= Tenofovir disoproxil fumarate; ATVr= Atazanavir/ritonavir; LPVr= Lopinavir/Ritonavir;
DRV/r=Darunavir/Ritonavir; DTG= Dolutegravir; RAL= Raltegravir; NGO=non-governmental organization; DBS= Dried blood spots; P refers to paediatric formulation while A refers to adult formulation in relation to Malawi Guidelines for Treatment of HIV in Adults and Children;
"/"is used for fixed dose combination; "+" is used for split dose combination

Factors associated to prevalence of HIV viral suppression among children and adults receiving ART in Malawi

We observed that 475,668 (92.8% of 515,797) patients had suppressed HIV VL. The factors associated with the prevalence of HIV viral suppression are shown in Table 2. The adjusted odds of HIV VL suppression among females receiving ART were 1.08 (95%CI: 1.05-1.11, P<0.001) times those of male receiving ART. Teenagers had the lowest probability of viral suppression (aOR=0.80, 95%CI: 0.75-0.85, P<0.001 compared with those aged 0-12 years) followed by those aged 20+ years (aOR=3.45, 95%CI: 3.27-3.65, P<0.001). The ART patients from urban clinics had a lower likelihood of HIV viral suppression than those living near rural clinics (aOR=0.95, 95%CI: 0.92-0.99, P=0.01). There was an increasing trend in HIV viral suppression with increasing ART duration (Table 2). Patients from faith-based health facilities had a higher prevalence of HIV viral suppression than patients from other types of health institutions. Patients with a plasma sample for HIV viral load monitoring were twice as likely to have a suppressed HIV viral load as those with DBS sample (aOR=2.42; 95%CI:2.20-2.66, P<0.001). Routine VL monitoring samples were 39% more likely to have HIV viral suppression than targeted HIV VL monitoring samples (aOR=1.39; 95%CI:1.34-1.43, P<0.001). After adjusting for age, sex, urban/rural location, duration on ART, regimen, reason for sample collection and type of sample (plasma vs. DBS sample), ART patients on ABC/3TC+RAL, TDF/3TC+ATVr and AZT/3TC+ATVr were less likely to have suppressed HIV viral load (Table 2).

Table 2: Factors associated with prevalence of HIV viral suppression among adults and children in Malawi in 2021

Patient characteristics (n = 515797)	n	Number of patients with HIV VL <1000 copies per ml	% of patients with of VL < 1000 copies per ml	Crude OR (95%CI)	P-value	Adjusted aOR (95%CI)	P-value
Total	**515,797**	475,668	92.8				
Gender							
Male	*181,127*	165,011	92.1	1.00		1.00	
Female	*299,951*	279,841	92.9	1.18 (1.15-1.20)	<0.001	1.08 (1.05-1.11)	<0.001
Location							
Rural	*323,998*	298,734	92.5	1.00		1.00	
Urban	*191,799*	176,934	92.9	1.08 (1.05-1.10)	<0.001	0.95 (0.92-0.99)	0.01
Age at sample draw (in years)							
0-12	*37,120*	267,75	76.5	1.00		1.00	
13-19	*23,617*	16,391	76.5	1.19 (1.14-1.24)	<0.001	0.80 (0.75-0.85)	<0.001
20+	*455,060*	432,502	94.6	6.03 (5.87-6.21)	<0.001	3.45 (3.27-3.65)	<0.001
Region							
Northern	*48,997*	45,193	92.2	1.00			
Central	*132,255*	122,219	93.0	1.17 (0.64-2.11)	0.64		
Southern	*334,545*	308,256	92.5	1.36 (0.78-2.38)	0.28		
Months on antiretroviral therapy							
6-11	*28,946*	25,348	89.8	1.00		1.00	
12-23	*30,600*	27,165	89.3	1.01 (0.96-1.07)	0.66	1.15 (1.07-1.23)	<0.001
24-35	*32,752*	30,295	91.1	1.13 (1.07-1.20)	<0.001	1.27 (1.18-1.36)	<0.001
36-47	*32,738*	29,362	91.8	1.28 (1.21-1.36)	<0.001	1.46 (1.36-1.57)	<0.001

48-59	*35,250*	33,263	92.5	1.30 (1.23-1.38)	<0.001	1.46 (1.36-1.57)	<0.001
60+	*237,424*	222,241	93.8	1.56 (1.50-1.68)	<0.001	1.59 (1.50-1.68)	<0.001
Managing authority of facility							
Faith-based	*86,329*	79,484	92.3	1.00		1.00	
Company	*4,546*	4,196	92.9	0.89 (0.78-1.00)	0.05	0.75 (0.64-0.89)	0.001
Government	*395,019*	364,702	92.7	0.99 (0.96-1.02)	0.42	0.94 (0.90-0.98)	<0.001
NGO	*9,819*	8,703	90.1	0.81 (0.76-0.88)	<0.001	0.93 (0.82-1.04)	0.20
Private	*20,084*	18,583	93.3	1.00 (0.94-1.07)	0.97	0.78 (0.71-0.86)	<0.001
Type of sample							
DBS	*437,716*	403,524	92.2	1.00		1.00	
Plasma	*78,081*	72,144	95.0	1.10 (1.05-1.14)	<0.001	2.42 (2.20-2.66)	<0.001
Reason for viral load sample							
Confirmatory	*44,491*	114,560	90.3	1.00		1.00	
Routine	*470,542*	361,108	93.4	1.62 (1.58-1.65)	<0.001	1.39 (1.34-1.43)	<0.001
ARV regimens							
0P (ABC/3TC+NVP)	*30*	24	80.0	1.00		1.00	
0A (ABC/3TC+NVP)	*39*	35	89.7	1.70 (0.43-6.72)	0.45	0.58 (0.08-4.34)	0.60
2P (AZT/3TC/NVP)	*978*	653	67.2	0.40 (0.16-0.99)	0.05	0.45 (0.17-1.18)	0.11
4A (AZT/3TC+EFV)	*225*	172	76.8	0.64 (0.25-1.66)	0.36	0.64 (0.23-1.80)	0.40
5A (TDF/3TC/EFV)	*1,773*	1,560	88.3	1.52 (0.61-3.80)	0.37	0.67 (0.25-1.77)	0.42
6A (TDF/3TC+NVP)	*167*	155	93.4	2.80 (0.94-8.31)	0.07	0.85 (0.20-3.55)	0.82
7A (TDF/3TC+ATVr)	*497*	382	77.2	0.68 (0.27-1.71)	0.41	0.26 (0.10-0.71)	0.01
8A (AZT/3TC+ATVr)	*952*	720	76.0	0.70 (0.28-1.75)	0.45	0.24 (0.09-0.64)	0.004
9P (ABC/3TC+LPVr)	*3,353*	2,078	62.1	0.35 (0.14-0.88)	0.025	0.44 (0.17-1.16)	0.10
9A (ABC/3TC+LPV/r)	*661*	480	73.0	0.57 (0.23-1.42)	0.23	0.42 (0.15-1.12)	0.08
10A (TDF/3TC+LPVr)	*201*	182	91.0	1.99 (0.72-5.56)	0.19	0.73 (0.15-3.65)	0.70
11P (AZT/3TC+LPVr)	*264*	215	81.4	0.86 (0.33-2.23)	0.75	0.36 (0.12-1.06)	0.06

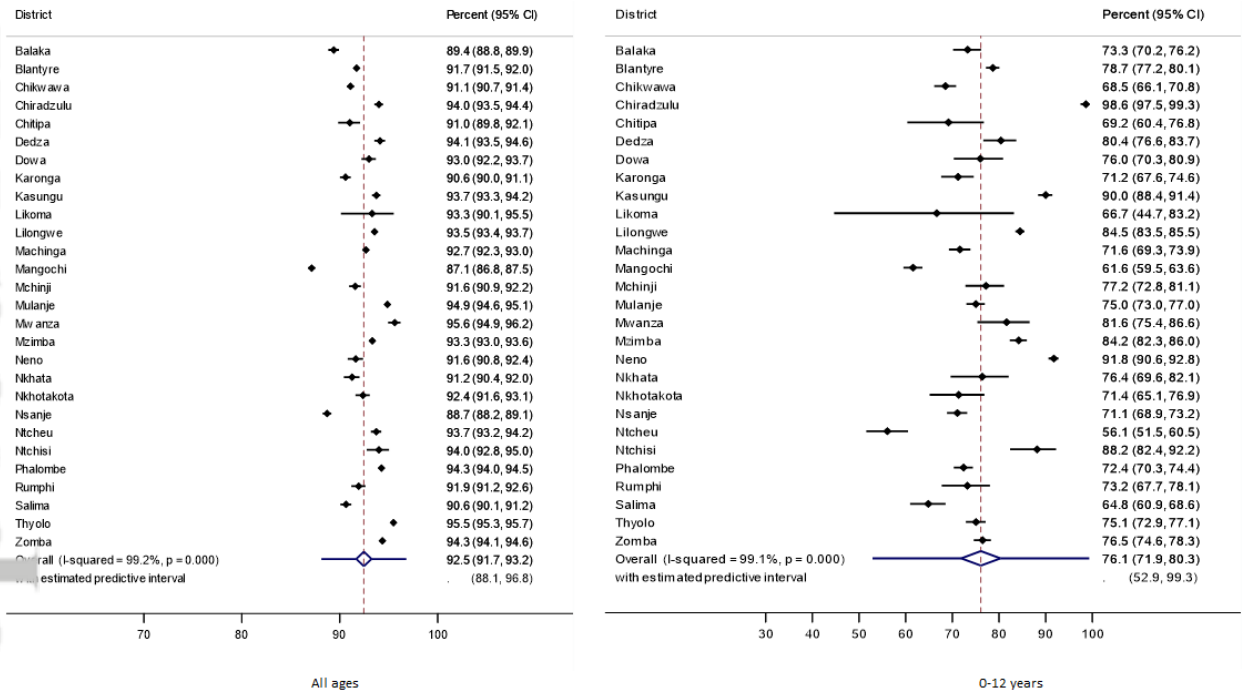
11A (AZT/3TC+LPVr)	*207*	191	92.3	2.47 (0.87-6.96)	0.09	1.24 (0.37-4.17)	0.73
12A (DRVr+DTG)	*622*	571	90.9	1.91 (0.75-4.91)	0.18	0.76 (0.28-2.10)	0.60
13A (TDF/3TC/DTG)	*322,483*	301,024	93.2	2.76 (1.12-6.80)	0.03	1.13 (0.43-2.97)	0.80
14P (AZT/3TC+DTG)	*191*	168	88.0	1.39 (0.51-3.79)	0.52	0.39 (0.10-1.44)	0.16
14A (AZT/3TC+DTG)	*2,534*	2,238	88.6	1.52 (0.61-3.77)	0.37	0.60 (0.23-1.58)	0.30
15P (ABC/3TC+DTG)	*2,145*	1,558	65.6	0.58 (0.23-1.44)	0.24	0.73 (0.28-1.91)	0.52
15A (ABC/3TC+DTG)	*2,520*	1,887	74.7	0.61 (0.25-1.51)	0.29	0.58 (0.22-1.52)	0.27
16P (ABC/3TC+RAL)	*80*	61	76.3	0.65 (0.23-1.85)	0.42	0.29 (0.08-0.99)	0.049

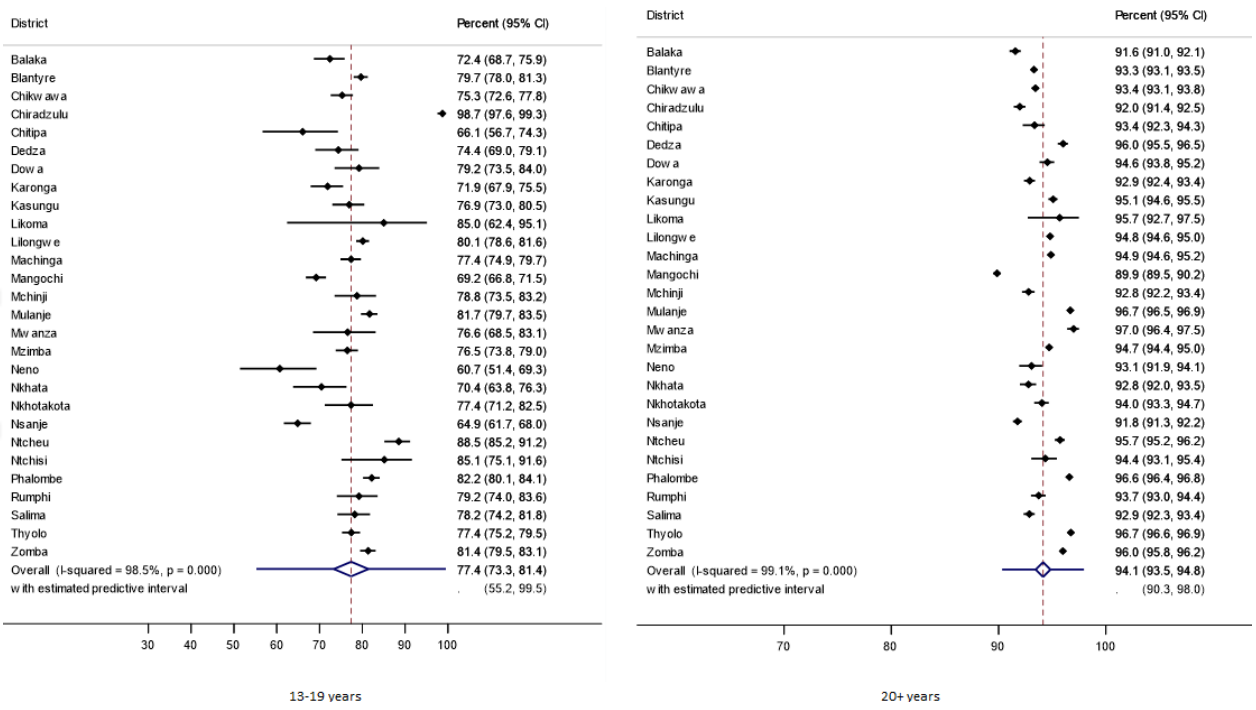
ABC= Abacavir; 3TC= Lamivudine; NVP= Nevirapine; AZT= zidovudine; EFV= efavirenz; TDF= Tenofovir disoproxil fumarate; ATVr= Atazanavir/ritonavir; LPVr= Lopinavir/Ritonavir;
DRV/r=Darunavir/Ritonavir; DTG= Dolutegravir; RAL= Raltegravir; NGO=non-governmental organization; DBS= Dried blood spots; OR=Crude Odds Ratio; aOR=Adjusted Odds Ratio; 95%CI=95% Confidence Interval; P refers to paediatric formulation while A refers to adult formulation in relation to Malawi Guidelines for Treatment of HIV in Adults and Children; /=is used for fixed dose combination +=is used for split dose combination

HIV viral suppression amongst adults and children in the districts of Malawi

The prevalence of HIV suppression across the districts of Malawi in 2021 is shown in Figure 1. There was a strong association between HIV viral suppression and district of residence (P<0.01). The within-district variability in the prevalence of HIV viral suppression was ρ=0.05 (95%CI: 0.02-0.09) in 2021. The prevalence of HIV viral suppression varied across the districts (σ=0.40; 95%CI: 0.28-0.57; P<0.001). Some districts had a prevalence of HIV viral suppression as high as 96% while in others it was as low as 87% in 2021. The three districts with the highest prevalence of HIV viral suppression among ART patients were Mwanza, Thyolo and Mulanje while the lowest prevalence of HIV viral suppression was observed in Mangochi, Nsanje and Balaka. There was spatial variation in the prevalence of HIV viral suppression across the different districts by age of the patients receiving ART (see Figure 1).

Figure 1: Spatial trends in the prevalence of HIV viral suppression amongst adults, adolescents and children in Malawi in 2021





95%CI=95% confidence interval

DISCUSSION

This is the first national analysis of HIV VL data from Malawi covering all health facilities providing antiretroviral treatment. We found that the overall prevalence of HIV viral suppression was 92.8% in 2021. Female sex, rural residency and prolonged time on ART were associated with an increase in prevalence of HIV viral suppression; and teenagers were the least likely and adults aged 20 years and above the most likely to have suppressed VL. Patients on ABC/3TC+RAL, TDF/3TC+ATVr and AZT/3TC+ATVr were the least likely to be virally suppressed, and although there was variation in prevalence of HIV viral suppression by district, HIV VL suppression rate in most districts was at least 90%.

Our study found a comparatively high rate of VL suppression, about 40% higher than what was reported overall in sub-Saharan Africa (SSA) by Nash et al [15].The difference between the two studies may be attributed to differences in the HIV viral suppression across different countries of SSA. The level of HIV viral load suppression was comparable to what has been reported in clinical trials: according to Havlir et al the rate of viral suppression was at least 87% in different trials conducted in Zambia, South Africa, Kenya, Uganda and Botswana [16]. This consistence in the HIV viral suppression with trial settings is an indication of successful implementation of the HIV programme by the Malawi's Department of HIV/AIDS. A study conducted in Rwanda also found high prevalence of HIV viral suppression in the era of HIV test and treat [17]. Therefore, the findings from Malawi are a demonstration of the successful implementation of the HIV test and treat policy suggesting that this policy can effectively contribute to attaining global HIV viral suppression targets [17] [18]. Another likely explanation for the high prevalence of HIV viral suppression could be the early introduction of routine VL monitoring in Malawi.

The study found that teenagers had the lowest level HIV viral suppression compared to the other age groups. This is similar to findings of Jiamsakul et al who also reported that children and adolescents had lower HIV viral suppression than

adults [19] although our paper reports current age whereas Jiamsakul reports age at ART initiation. A study from Rwanda also found that those in their teens were less likely to have HIV viral suppression and the older patients having higher likelihood of HIV viral suppression [17]. A multi-country study using data from Population-based HIV Impact Assessment (PHIA) across SSA also found that teenagers had lower HIV viral suppression probability than other age groups [18]. As many teenagers attend boarding schools there is a need to involve the school management so that they help ensure that ARV medications are consistently taken by this population, although this should be balanced against inadvertent HIV status exposure in Malawi. Furthermore, there is evidence from Uganda suggesting that improved economic security is associated with better HIV viral suppression among adolescents [20].

Our findings also demonstrate differences in prevalence of HIV viral suppression between rural and urban areas, people in urban regions having lower prevalence of HIV viral suppression than the rural population. This is inconsistent to what was observed in Ethiopia [21] where the urban population receiving ART had a higher likelihood of HIV viral suppression than the rural population. Some high-income countries like the USA demonstrate no statistically significant rural-urban differences in HIV viral suppression [22]. The difference observed in SSA could be due to differences in the HIV/AIDS health system designs in these settings. In Malawi, HIV prevalence is much higher in urban than in rural areas as reported in the Malawi PHIA. Other explanations for the lower prevalence of HIV viral suppression in urban areas may include high in-migration that is coupled with treatment interruptions or lack of transport to the clinic for patients [24] as well as patients being busier with economic activities for their livelihood in urban areas hence skipping their ART appointments and consequently having higher rates of HIV VL rebound amongst the urban population. Therefore, introducing longer opening of clinics in urban areas as well as introduction of care groups for ART pick-up may improve ART adherence and consequently increase HIV viral suppression.

We also found that females were more likely to have HIV viral suppression than males as reported in RSA [25]; Ethiopia[21] and Eswatini, Lesotho, Malawi, Zambia and Zimbabwe [7], [25], [21]. This may be due to that fact that males interrupted treatment more often than females [18]. Introduction of ART clinics with prolonged opening hours may help cover this gap by ensuring that most of the men have access to antiretrovirals and hence having suppressed HIV VL. In addition, women tend to start ART earlier than males hence the higher likelihood of women to have higher prevalence of HIV viral suppression. Further, the acceptability of ART services provided outside the usual opening hours by the male population could be assessed before their implementation.

Consistently with studies conducted in RSA[25]; Ethiopia[21] and Eswatini, Lesotho, Malawi, Zambia and Zimbabwe [7] [26] we found that the prevalence of HIV viral suppression increased with the duration on ART. This has practical implications for the introduction of enhanced and targeted ART adherence counselling, especially amongst persons who have just started ART. Other studies have quoted the presence of antiretroviral-related side-effects as being the key barrier to unsuppressed HIV VL amongst the persons on ART.

We observed variation in HIV viral suppression by type of ARV regimens taken by the individuals. A multicountry study using data from PHIA in SSA also found that the ARV regimens were associated with HIV viral suppression compared to the other age groups [18]. The Malawi DHA needs to investigate why the patients on TDF/3TC+ATVr, AZT/3TC+ATVr and ABC/3TC+RAL had the least likelihood of HIV viral suppression. However, in our analysis we did not distinguish between the use of regimens as 1st/2nd/3rd line due to unavailability of data by regimen line.

The limitations of this study include missing data on TB status. Furthermore, it was difficult to interpret routine scheduled and targeted follow-up HIV VL results in the same analysis, particularly since we could not reliably identify subsequent samples from the same patients from the Malawi LIMS. Due to the protocol that someone with high HIV VL on a routine monitoring sample is supposed to get intensive adherence counselling and a follow-up sample, there is a high probability that patients with a high initial VL are represented with two or more subsequent high results. It is therefore challenging to interpret and extrapolate from this because it was difficult to link some of the HIV VL results for some patients since the ART identification information were not captured consistently into the LIMS. Another limitation is that our findings on HIV VL suppression prevalence may not be generalizable to patients who had no HIV viral load measurement.

The main strength of this study is that nationally representative routine programme HIV data were used, which increases the potential of the findings to inform the HIV programmes on sustaining the high HIV viral suppression in Malawi and other similar settings. The study also has implications on improving the programmatic documentation especially for the inclusion of key variables like TB status.

CONCLUSIONS

This is the first national analysis of HIV VL data from the laboratory database management system covering all the health facilities providing antiretroviral treatment in Malawi in 2021. The finding of high HIV viral suppression in individuals on ART in this study has implications for HIV management. Our findings show the need to consider in particular urban residents, those aged below 20 years, males, those on ART for less than a year and those on certain ARV regimens in order to persistently suppress HIV VL and consequently achieve the goal of achieving HIV VL suppression by 2030.

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REFERENCES

[1] E. Zaniewski *et al.*, "Trends in CD4 and viral load testing 2005 to 2018: multi-cohort study of people living with HIV in Southern Africa," *J. Int. AIDS Soc.*, vol. 23, no. 7, pp. 1–10, 2020, doi: 10.1002/jia2.25546.

[2] WHO, "Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV," *WHO*, 2016.

[3] WHO, *Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy*, 2017th ed., vol. 2. WHO, 2017.

[4] World Health Organization, "2018 Global Reference List of 100 Core Health Indicators (plus health-related SDGs)," *WHO*, 2018, [Online]. Available: https://apps.who.int/iris/bitstream/handle/10665/259951/WHO-HIS-IER-GPM-2018.1-eng.pdf?sequence=1.

[5] W. Ng'ambi, I. K. Chiumia, N. Chagoma, and J. Mfutso-bengo, "Factors Associated with Uptake of HIV Testing in Malawi : A Trend Analysis of the Malawi Demographic and Health Survey Data from 2004 to 2016," *J. HIV AIDS Res.*, vol. 2, no. 1, pp. 1–10, 2020.

[6] L. Bulage *et al.*, "Factors Associated with Virological Non-suppression among HIV-Positive Patients on Antiretroviral Therapy in Uganda, August 2014-July 2015," *BMC Infect. Dis.*, vol. 17, no. 1, pp. 1–11, 2017, doi: 10.1186/s12879-017-2428-3.

[7] A. D. Haas *et al.*, "Prevalence of nonsuppressed viral load and associated factors among HIV-positive adults receiving antiretroviral therapy in Eswatini, Lesotho, Malawi, Zambia and Zimbabwe (2015 to 2017): results from population-based nationally representative surveys," *J. Int. AIDS Soc.*, vol. 23, no. 11, pp. 1–12, 2020, doi: 10.1002/jia2.25631.

[8] MoH, "Government of Malawi Ministry of Healt, Malawi Integrated Guidelines for Clinical Management of HIV, 2016th ed., vol. 2016."

[9] MoH, *The 4th Edition of the Malawi Integrated Guidelines and Standard Operating Procedures for Clinical HIV Services*, vol. 151, no. 2. 2018.

[10] MoH, "2019 Policy Updates: Addendum to the 4th Edition of the Malawi Integrated Guidelines and Standard Operating Procedures for Clinical HIV Services," 2019.

[11] Malawi Ministry of Health, "Government of Malawi Ministry of Health Integrated HIV Program Report April - June 2021," no. June, pp. 1–37, 2021.

[12] MoH, "'Department of HIV/AIDS Management Information System'. Ministry of Health, Malawi."

[13] S. Nicholas *et al.*, "Point-of-care viral load monitoring : outcomes from a decentralized HIV programme in Malawi," pp. 1–9, 2019, doi: 10.1002/jia2.25387.

[14] S. L. Lecher *et al.*, "HIV Viral Load Monitoring Among Patients Receiving Antiretroviral Therapy — Eight Sub-Saharan Africa Countries, 2013–2018," *MMWR. Morb. Mortal. Wkly. Rep.*, vol. 70, no. 21, pp. 775–778, 2021, doi: 10.15585/mmwr.mm7021a2.

[15] D. Nash, M. Yotebieng, and A. H. Sohn, "Treating all people living with HIV in sub-Saharan Africa: a new era calling for new approaches," *J. Virus Erad.*, vol. 4, pp. 1–4, 2018, doi: https://doi.org/10.1016/S2055-6640(20)30340-X.

[16] D. Havlir *et al.*, "What do the Universal Test and Treat trials tell us about the path to HIV epidemic control?," *J. Int. AIDS Soc.*, vol. 23, no. 2, p. e25455, Feb. 2020, doi: https://doi.org/10.1002/jia2.25455.

[17] J. Ross *et al.*, "High levels of viral load monitoring and viral suppression under Treat All in Rwanda – a cross-sectional study," *J. Int. AIDS Soc.*, vol. 23, no. 6, p. e25543, 2020, doi: https://doi.org/10.1002/jia2.25543.

[18] A. D. Haas *et al.*, "Prevalence of nonsuppressed viral load and associated factors among HIV-positive adults receiving antiretroviral therapy in Eswatini, Lesotho, Malawi, Zambia and Zimbabwe (2015 to 2017): results from population-based nationally representative surveys," *J. Int. AIDS Soc.*, vol. 23, no. 11, p. e25631, Nov. 2020, doi: https://doi.org/10.1002/jia2.25631.

[19] and M. L. Awachana Jiamsakul, Azar Kariminia, Keri N Althoff, Carina Cesar, Claudia P Cortes, Mary-Ann Davies, Viet Chau Do, Brian Eley, John Gill, Nagalingeswaran Kumarasamy, Daisy Maria Machado, "antiretroviral therapy – results from the IeDEA collaboration," *J Acquir Immune Defic Syndr*, vol. 76, no. 3, p. 5, 2020, doi: 10.1097/QAI.0000000000001499.HIV.

[20] L. G. Bermudez *et al.*, "Does Economic Strengthening Improve Viral Suppression Among Adolescents Living with HIV? Results From a Cluster Randomized Trial in Uganda," *AIDS Behav.*, vol. 22, no. 11, pp. 3763–3772, 2018, doi: 10.1007/s10461-018-2173-7.

[21] G. Diress, S. Dagne, B. Alemnew, S. Adane, and A. Addisu, "Viral Load Suppression after Enhanced Adherence Counseling and Its Predictors among High Viral Load HIV Seropositive People in North Wollo Zone Public Hospitals, Northeast Ethiopia, 2019: Retrospective Cohort Study," *AIDS Res. Treat.*, vol. 2020, p. 8909232, 2020, doi: 10.1155/2020/8909232.

[22] S. Weissman, W. A. Duffus, M. Iyer, H. Chakraborty, A. V. Samantapudi, and H. Albrecht, "Rural-urban differences in HIV viral loads and progression to AIDS among new HIV cases.," *South. Med. J.*, vol. 108, no. 3, pp. 180–188, Mar. 2015, doi: 10.14423/SMJ.0000000000000255.

[23] M. Ministry of Health, "MPHIA 2015-2016 Collaborating Institutions," pp. 2–70, 2017.

[24] H. Tweya *et al.*, "Are They Really Lost? 'True' Status and Reasons for Treatment Discontinuation among HIV Infected Patients on Antiretroviral Therapy Considered Lost to Follow Up in Urban Malawi," *PLoS One*, vol. 8, no. 9, 2013.

[25] S. Africa, "HHS Public Access," vol. 29, no. 6, pp. 603–610, 2020, doi: 10.1177/0956462417748859.Factors.

[26] T. Apollo, K. C. Takarinda, A. Phillips, C. Ndhlovu, and F. M. Cowan, "Provision of HIV viral load testing services in Zimbabwe: Secondary data analyses using data from health facilities using the electronic Patient Monitoring System," *PLoS One*, vol. 16, no. 1, p. e0245720, Jan. 2021, [Online]. Available: https://doi.org/10.1371/journal.pone.0245720.

[27] M. B. Shiferaw *et al.*, "Viral suppression rate among children tested for HIV viral load at the Amhara Public Health Institute, Bahir Dar, Ethiopia," *BMC Infect. Dis.*, vol. 19, no. 1, p. 419, 2019, doi: 10.1186/s12879-019-4058-4.

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